

Attorney Docket No. 960296.99179
Applicants: Thomson et al.
Filed: 25 July 2003
U.S. Application No.: 10/627,245
Art Unit: 1636
Date of Office Action: 11 July 2007
Amendment Dated: 31 October 2007
Examiner: Daniel M. Sullivan

REMARKS

In an Office Action mailed July 11, 2007, the Examiner in charge of the application withdrew a rejection under 35 U.S.C. § 112, second paragraph of the pending claims. The Examiner maintained rejections under 35 U.S.C. § 103(a) of the pending claims as being unpatentable over Priori *et al.* (1996) in view of Gepstein *et al.* (evidenced by US provisional application 60/306,462). The Examiner imposed a new ground of objection to Claims 7, 10 and 13 for language informality.

The rejections were made final. A Request for Continued Examination accompanies this response so the finality of the rejection will be withdrawn. Each issue raised by the Examiner is addressed separately below.

New Ground of Objection

The objections raised to Claim 7, 10 and 13 are addressed by the indicated amendments and reconsideration is respectfully requested.

Amendment to Clarify Claim 13

Claim 13 is amended to clarify that separate insertions and measurements are intended. Support for the amendment is found in paragraph [00046] of the application as filed.

Rejections Under 35 U.S.C. § 103

The Examiner maintained the rejections for alleged obviousness asserting that Gepstein *et al.* teaches “deriving a plurality of cardiomyocyte types by *in vitro* culture from human embryonic stem cells.” The Examiner asserted that the morphological differences identified by Gepstein *et al.* were sufficient to demonstrate a plurality of cardiomyocyte cell types at any ratio or in any number. Further the Examiner contended that Gepstein *et al.* would provide the skilled person with a reasonable expectation of success in deriving the claimed plurality of cardiomyocyte types, noting his belief that the same would be true even if the claim were construed to require atrial, ventricular or nodal cardiomyocyte types.

The independent claims now recite that after *in vitro* culture of embryoid bodies derived from human embryonic stem cells for between 40 and 95 days, atrial-, ventricular- and nodal

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cardiomyocyte cell types are derived. At least this element of the claims is not reasonably predictable from the Gepstein *et al.* application.

Applicants' remarks in response to the prior Office Action, especially as to Gepstein *et al.*'s failure to assess their cardiomyocytes and the distinctions between mouse and human development, are incorporated and reiterated as if set forth here again.

Further, Gepstein *et al.* cultured their embryoid bodies for no more than 30 days and stressed repeatedly the early nature of the cardiomyocytes in their cultured embryoid bodies. Gepstein *et al.* provided no indication that the three recited cell types are present in the culture and pointed only to morphological differences among cells in the embryoid bodies, with no characterization of any lineage commitment among those morphologically distinct cells. While a person skilled in the field of cardiac cellular developmental biology understands that cardiomyocytes undergo lineage specification during development, nothing in Gepstein *et al.* indicates whether any identified morphological difference associated with myocytes from the embryoid body precedes or follows lineage specification. Accordingly, the skilled person cannot determine whether the early Gepstein *et al.* cardiomyocytes reflect differences that precede lineage specification, reflect differences within a single lineage after lineage specification, or reflect some other situation. Because Gepstein *et al.* did not measure the action potential of individual cells, that application provides no basis for asserting the presence of distinct cardiomyocyte cell types, or even whether the given culture conditions would suffice to derive the recited cell types.

The emerging field of cellular developmental biology, especially at it concerns individual cell development, was inherently unpredictable when the application was filed, and remains unpredictable today. Against this background, then, the Examiner refers in passing to an alleged teaching of Gepstein *et al.* that "*in vitro* differentiation of human and mouse ES cells appears to follow parallel pathways" (page 14, lines 3-4). Applicants question what this sentence 'teaches' the skilled person. It is no substitute for, and certainly no proof of, the statement's accuracy, nor can it suffice as definitive evidence of a reasonable expectation of success in this unpredictable

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art. Often, the very basis for invention arises when an initial appearance of similarity is shown to be incorrect.

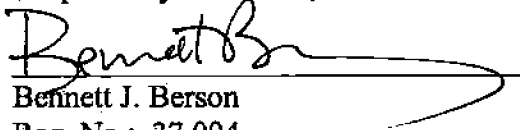
In summary, the Examiner's rejections for obviousness premised upon a skilled person's reasonable expectation of success are untenable and cannot stand, in view of (1) the unpredictability of the field as of the filing date, (2) the acknowledged differences between murine and human cardiac development, (3) the absence of any concrete or compelling evidence of a parallel pathway to the murine system in humans, (4) the limited term of the Gepstein *et al.* cultures, and (5) the express recitation by Applicants of longer term culture conditions and three distinct cell types.

Reconsideration is respectfully requested.

Fees

A petition for an extension of time for one month accompanies this response so the response will be deemed to have been timely filed. Should any additional extension of time be due, in this or in any subsequent response, please consider this to be a petition for the appropriate extension of time and a request to charge the petition fee to deposit account number 17-0055. No other fee apart from the fee for the Request for Continued Examination is believed due. However, should any be due in this or any subsequent response, please consider this a request to charge the fee to the same deposit account.

Respectfully submitted,



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